CLAIMS

1. A method of modulating the immune response in a patient in need of such modulation, the method comprising administering to the patient an effective amount of an inhibitor of asparaginyl endopeptidase.

2. A method according to Claim 1 wherein the patient has or is at risk of a disease which involves MHC Class II molecules.

3. A method according to Claim 1 or 2 wherein the disease is an autoimmune disease.

4. A method according to Claim 3 wherein the disease is rheumatoid arthritis.

5. A method according to Claim 1 or 2 wherein the patient has or is at risk of an allergic or hypersensitivity reaction.

6. A method according to Claim 1 or 2 wherein the patient has undergone or is to undergo a transplant.

7. A method according to Claim 6 wherein the material transplanted, or to be transplanted, has been contacted with an effective amount of an inhibitor of asparaginylendopeptidase.

8. A method according to any one of the preceding claims wherein the inhibitor is a competitive inhibitor.

9. A method according to Claim 8 wherein the competitive inhibitor is a peptide comprising is an asparagine-containing peptide.

10. A method according to Claim 9 wherein the peptide is an N and C-terminal blocked peptide Ala-Glu-Asn-Lys-NH (AENK) or Lys-Asn-Asn-Glu-NH (KNNE).

11. A method according to Claim 1 to 6 wherein the inhibitor is a non-competitive or irreversible inhibitor.

12. A method according to Claim 11 wherein the inhibitor has the structure Bl-$(X)_n$-Asn-Q where Bl is any suitable N terminal blocking group; X is an amino acid residue; n is between 1 and 100, Asn is an asparagine residue and Q is a group capable of reacting with the active site cysteine of asparaginyl endopeptidase.

13. A method according to any one of the preceding claims further comprising administering to the patient an effective amount of an agent for treatment or prevention or amelioration of an autoimmune disease or an allergic or hypersensitivity reaction.

14. A method according to any one of Claims 1 to 12 further comprising administering to the patient an effective amount of an immunosuppressive agent.

15. A method of reducing the processing of a protein antigen by a MHC Class II molecule by a cell, the method comprising contacting the cell with an inhibitor of asparaginyl endopeptidase.

16. A method according to Claim 15 wherein the inhibitor is a competitive inhibitor.

17. A method according to Claim 16 wherein the competitive inhibitor is a peptide comprising an asparagine-containing peptide.

18. A method according to Claim 17 wherein the peptide is an N and C-terminal blocked peptide Ala-Glu-Asn-Lys-NH (AENK) or Lys-Asn-Asn-Glu-NH (KNNE).

19. A method according to Claim 15 wherein the inhibitor is a non-competitive or irreversible inhibitor.

20. A method according to Claim 19 wherein the inhibitor has the structure Bl-$(X)_n$-Asn-Q where, Bl is any suitable N terminal blocking group; X is an amino acid residue; n is between 1 and 100, Asn is an asparagine residue and Q is a group capable of reacting with the active site cysteine of asparaginyl endopeptidase.

21. A method according to any one of Claims 15 to 20 wherein the cell is, or is comprised in a tissue or organ, for transplantation into a patient.

22. Use of an inhibitor of asparaginyl endopeptidase in the manufacture of a medicament for modulating the immune response in a patient in need of such modulation.

23. Use according to Claim 22 wherein the patient has or is at risk of a disease which involves MHC Class II molecules.

24. Use according to Claim 22 or 23 wherein the disease is an autoimmune disease.

25. Use according to Claim 24 wherein the disease is rheumatoid arthritis.

26. Use according to Claim 22 or 23 wherein the patient has or is at risk of an allergic or hypersensitivity reaction.

27. Use according to Claim 22 or 23 wherein the patient has undergone or is to undergo a transplant.

28. Use according to any one of Claims 22 to 27 wherein the inhibitor is a competitive inhibitor.

29. Use according to Claim 28 wherein the competitive inhibitor is a peptide comprising is an asparagine-containing peptide.

30. Use according to Claim 29 wherein the peptide is an N and C-terminal blocked peptide Ala-Glu-Asn-Lys-NH (AENK) or Lys-Asn-Asn-Glu-NH (KNNE).

31. Use according to any one of Claims 22 to 27 wherein the inhibitor is a non-competitive or irreversible inhibitor.

32. Use according to Claim 31 wherein the inhibitor has the structure Bl-$(X)_n$-Asn Q where Bl is any suitable N terminal blocking group; X is an amino acid residue; n is between 1 and 100, Asn is an asparagine residue and Q is a group capable of reacting with the active site cysteine of asparaginyl endopeptidase.

33. Use according to any one of Claims 22 to 32 wherein the patient is administered an effective amount of an agent for treatment or prevention or amelioration of an autoimmune disease or an allergic or hypersensitivity reaction.

34. Use according to any one of Claims 22 to 32 wherein the patient is administered an effective amount of an immunosuppressive agent.

35. Use of an inhibitor of asparaginyl endopeptidase for modulating the immune response in a patient in need of such modulation.

36. Use of an inhibitor of asparaginyl endopeptidase for reducing the processing of a protein antigen by a MHC Class II molecule by a cell.

37. An inhibitor of asparaginyl endopeptidase for use in medicine.

38. A pharmaceutical composition comprising an inhibitor of asparaginyl endopeptidase and a pharmaceutically acceptable carrier.

39. A pharmaceutical composition according to Claim 38 further comprising an agent which is usefully administered to a patient in need of modulation of the immune response.

40. A pharmaceutical composition according to Claim 38 further comprising an agent for treatment or prevention or amelioration of an autoimmune disease or an allergic or hypersensitivity reaction.

41. A pharmaceutical composition according to Claim 38 further comprising an immunosuppressive agent.

42. A pharmaceutical composition comprising an inhibitor of asparaginyl endopeptidase, an inhibitor of cathepsin S and a pharmaceutically acceptable carrier.

43. A method of identifying a compound for modulating Class II MHC antigen processing the method comprising contacting a test compound with asparaginyl endopeptidase and selecting a compound which reduces its activity.

44. A method according to Claim 43 wherein the activity of asparaginyl endopeptidase is measured using a substrate which upon cleavage by said endopeptidase, yields a readily detectable product.

45. A method according to Claim 44 wherein the substrate is Z-Ala-Ala-Asn-7-(4-methyl)coumarylamide and the product is fluorescent.

46. A method according to any one of Claims 43 to 45 the method further comprising the step of determining whether the so selected compound is capable of substantially inhibiting the loading and

presentation of peptides on an appropriate Class II MHC molecule-containing cell.

47. A method according to Claim 46 wherein it is determined whether the so selected compound is capable of substantially inhibiting T cell activation by an appropriate Class II MHC molecule-containing cell.

48. A non-human transgenic animal wherein a gene encoding asparaginyl endopeptidase has been modified and the animal expresses substantially no asparaginyl endopeptidase from said gene.

49. A non-human transgenic animal according to Claim 48 which is a mouse.

50. A non-human transgenic animal according to Claim 48 or 49 further comprising a genetic background which predisposes to an autoimmune disease either spontaneously or upon administration of protein antigen.

51. A non-human transgenic animal according to Claims 48 or 49 further transgenic for a human Class II MHC molecule and, optionally, further transgenic for human CD4.

52. An inhibitor of asparaginyl endopeptidase which has the structure Bl-(X_a-X_n)-Asn-Q wherein Bl is any suitable N terminal blocking group; X_a-X_n are the n amino acid residues immediately N terminal to an Asn cleavage site in the invariant chain of Class II MHC molecules; Asn is an

asparagine residue; and Q is a group capable of reacting with the active site of asparaginyl endopeptidase.

53. An inhibitor according to Claim 52 wherein the number of amino acid residues in (X_a-X_n) is between 1 and 25, preferably between 2 and 10.

54. An inhibitor according to Claim 53 which is any of Bl-Ser-Gln-Asn-Q; Bl-Leu-Glu-Asn-Q; Bl-Leu-Gln-Asn-Q; Bl-Pro-Glu-Asn-Q; Bl-Leu-Lys-Asn-Q; Bl-Gln-Asn-Q; Bl-Glu-Asn-Q; Bl-Asp-Glu-Asn-Q; Bl-Asn-Gly-Asn-Q; Bl-Phe-Pro-Asn-Q; Bl-Val-Pro-Asn-Q; and Bl-His-His-Asn-Q.

55. An inhibitor of asparaginyl endopeptidase which has the structure (Xb-Xc)Asn(Xd-Xe) wherein (Xb-Xc) are the r amino acid residues immediately N terminal to an Asn cleavage site in the invariant chain of Class II MHC molecules and (Xd-Xe) are the s amino acid residues immediately C terminal to an Asn cleavage site in the said invariant chain; Asn is an asparagine residue; and r and s are independently between 2 and 25, provided that the inhibitor is not the peptide CVFPNGTEVPNTRSRGHHN or the peptide ATKYGNMTEDHVMHLLQNA.

56. A composition comprising an inhibitor of asparaginyl endopeptidase and an inhibitor of cathepsin S.